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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/746,581	12/21/2000	Therese Jourdier	00,1287	1597

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	8

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/746,581	JOURDIER ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- Th MAILING DATE of this communication appears on th cov r sheet with the corr spond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) *6 and 7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 6 and 7 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

Priority

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on March 16, 2001, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

5. The disclosure is objected to because of the following informalities: On pages 15-16, it appears as though a portion of the disclosure, possibly the material later restated in the table on pages 17 and 18, is absent. A corrected explanation of Example III is requested. Note, material

not part of the original application as filed will be considered New Matter thereto. Appropriate correction is required.

Claim Objections

6. Claims 5 and 8 are objected to because of the following informalities: the claims identify the immunogen as being from the HIV virus. The term "virus" is redundant as "HIV" stands for human immunodeficiency virus. It is suggested that the claims be amended to read on methods wherein the pathogen is, or the immunogen is an immunogen against, HIV. Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-5, 8, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is treated as representative of the identified claims. This claim reads on methods of producing a local immunogenic response against a pathogen, including where the pathogen is HIV, by administration of a vaccine composition. The claim is unclear due to the limitation requiring that the response be raised by the administration of a "vaccine composition." The term "vaccine" generally implies that the composition is capable of raising a protective response. See e.g., Stedman's Online Medical Dictionary (defining "vaccine" as a preparation intended to raise a prophylactic response). This definition is in contrast to the term immunogenic, which does not necessarily imply that the response raised is protective. See

Stedman's, definitions for "antigen" and "immunogen." Thus, while it appears as though the claim was intended to read on immunogenic responses generally, the reference to the use of a vaccine composition makes it unclear as to whether the claim is intended to read only on the induction of protective responses, or if the claim is, in fact, intended to read on any immunogenic response.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-5, 8, and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of producing local immunogenic responses against HIV, does not reasonably provide enablement for embodiments wherein a protective response is being raised against HIV. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The Claims have been described above. As was indicated above, the present claim language implies that the claimed method is inducing a protective response against the target pathogen. For the purposes of the present rejection, it is being assumed that the claims were intended to read on methods of inducing such a protective response. Because the claims further identify HIV as a target antigen, the claims broadly read on methods of inducing localized protective responses against HIV.

In the application, the Applicant has provided no evidence that the claimed methods are capable of inducing a protective response against HIV. The examples and data provided in the specification demonstrate that the claimed methods are capable of eliciting the production of IgA antibodies, but not that the antibodies are protective. See, pages 14-21. Thus, the Applicant has provided no working examples, and little guidance, that would lead those in the art to operative methods of inducing protective anti-HIV responses.

In addition to the lack of enabling support in the specification for claims reading on the induction of a protective anti-HIV response, the art further indicates that the Applicant is not enabled for such methods. For example, each of the references of Schnell et al. (PNAS 97: 3544-49, at 3544), Pang et al. (BMC Microbiol 1(1): 28, page 1), and Doria-Rose et al. (J Virol 77: 11563-77, at 11563) teach that, while there have been advances in the development of anti-HIV therapies, the art is still in need of an effective anti-HIV vaccine. In part, this need stems from the recognized challenges that those in the art face in attempting to make such vaccines. See e.g., Pang, page 2. Thus, the art teaches that, despite the high skill of those in the art, the complexity and unpredictability of the art have prevented those in it from producing an effective anti-HIV vaccine. In view of the limited teachings by the Applicant over the prior art with respect to such vaccines, the application has not provided an enabling disclosure for the methods as currently claimed.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1- 3, 5, 8, and 9 rejected under 35 U.S.C. 102(b) as being anticipated by Thibodeau et al., (C R Acad Sci, Paris 313: 389-94- of record in the IDS of March 2001). The claims have been described above. For the purposes of this rejection, it is being assumed that the claimed methods do not requires the induction of protective response against HIV. Thibodeau teaches the induction of secretory IgA antibodies in rabbits through the application of HIV antigen (comprising gp160) to the oral mucosa. Page 390. It is noted that, while the reference teaches that further parenteral immunization was required for induction of IgG and IgM, s-IgA was locally induced after repeated contacts of the immunogenic composition to the oral mucosa. Page 390, last paragraph. The reference therefore anticipates the identified claims.

13. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Gaffar et al. (U.S. Patent 3,931,398- submitted in the IDS of March 2001). The claims read generally on methods of producing a local secretory IgA response against pathogens through oral administration of an antigen against the pathogen. Gaffar teaches such a method. Abstract, cols. 3-4. The reference therefore anticipates the identified claims.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1-3, 5, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thibodeau as applied to claims 1-3, 5, 8, and 9 above, and further in view of Mathiowitz et al. (U.S. Patent 6,235,313) and Irwin et al. (WO 96/20731- of record in the March 2001 IDS). Thibodeau was described above. It teaches that oral administration of an HIV antigen to induce a local secretory IGA response. Mathiowitz demonstrates that the use of bioadhesives was known for the delivery of drugs. Irwin describes formulations that may be used for oral delivery, including those with bioadhesives. Page 36. While Irwin is primarily concerned with the delivery of genetic vaccines, one of ordinary skill in the art would have been aware that such general formulations would be equally applicable with other antigen types, including the proteins of Thibodeau.

16. Claims 1-5, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thibodeau as applied to claims 1-3, 5, 8, and 9 above, and further in view of either Lowell et al. (J Infect Dis 175: 292-301), or Gandhi et al. (Adv Drug Deliv Rev, 13: 43-74). The claims other than claim 4 have been described above. Claim 4 specifies that the bioadhesive or capsule comprising the antigen either further comprises, or is coupled to, a system to promote penetration of the immunogenic composition. The Teachings of Thibodeau have been described above. The

reference teaches only the oral administration of the antigen (read as deposition), as does not teach the use of penetration enhancers.

Lowell teaches that the use of certain formulations may be used to enhance the uptake of antigens in mucosal vaccines for antigen processing and presentation, thereby enhancing the immunogenicity of the antigens. Page 298. Gandhi teaches both various forms of administering oral doses of vaccines (pages 44-45, and 53), and the use of penetration enhancers to overcome some of the problems involved in the delivery of peptidic antigens. Page 64. From either of these references, it would have been obvious to one of ordinary skill in the art to use such alternative formulations for the delivery of the antigen of Thibodeau. The references therefore render the identified claims obvious.

17. Claims 1-5, 8, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hinkula et al. (Vaccine 15: 874-78- of record in the IDS of March 2001) in view of Irwin and Beckenkamp (HNO 33:196-203), and further in light of the teachings of Kozlowski et al. (Infect Immun 65(4): 1387-94), and Gorse et al. (Clin Diag Lab Immunol 3(6): 769-73). The claims have been described above. It is noted that on pages 8-9 of the specification, the term immunogenic composition has been defined as including recombinant vaccines. Thus, the term immunogen in the claims is read as including polynucleotides that encode protein antigens.

Hinkula teaches the use of recombinant antigens. Including a version encoding the gp160 of HIV, to induce expression of anti-HIV IgA. Abstract, page 874. However, while the reference does teach administration in the oral cavity, it does not teach the administration of the antigen to the floor the subject's mouth.

Irwin teaches, as indicated above, formulations that may be used to administer recombinant vaccines into the oral cavity. Page 36. The reference further teaches that the delivery vehicles disclosed therein may be used for the delivery of the HIV gp160 antigen. Pages 4-5. Irwin also teaches the formulations may be formulated to allow for enhanced absorption (i.e.- penetration) of the vaccine. Thus, it would have been obvious to one of ordinary skill in the art to orally administer a recombinant vaccine composition encoding the HIV gp160 antigen to induce the expression of anti-HIV antibodies. However, the identified references neither provide a motivation for doing so, nor specifically render obvious the administration of the composition to the floor of the subject's mouth.

Kozlowski teaches that secretory IgA antibodies are an important factor in effective vaccination against sexually transmitted diseases. Page 1387. Gorse teaches that such antibodies are important in the inhibition of HIV infection in particular. Gorse further teaches that the induction of such antibodies in the mucosal membranes of the mouth are important due to the oral transmissibility of the virus. Thus, the teachings of these two references provide both a suggestion and motivation to induce the expression of anti-HIV secretory IgA in a subject.

Finally, the Beckenkamp reference teaches that, in the mouth, there are several areas that, when contacted with an antigen, will produce IgA antibodies against the antigen. (English Summary, page 196). While the reference teaches that the floor of the mouth is not the most responsive region of the mouth, the reference does teach that the cells in this region will produce IgAs. Thus, from the cumulative teachings of these references, it would have been obvious to one of ordinary skill in the art to perform the claimed methods to induce an anti-HIV IgA response.

18. Claims 1-5, 8, and 9 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Becker et al. (U.S. Patent 6,379,675) in view of Gorse and Beckenkamp. The claims have been described above. Becker teaches that local secretory IgA antibodies may be elicited by a local application of an antigen to a mucosal site. Cols. 12-13. Among the antigens disclosed by the reference is the gp160 protein of HIV. Col. 10, lines 25-68, esp. lines 48-49. Becker further teaches that compositions that may used to induce such a response may be administered orally, and mucosally (including perlingually). Col. 14, lines 19-38. These compositions may include addition components to enhance absorption (penetration) of the antigen across the mucosal membranes. Cols 14-15. Finally, the reference also teaches that the composition may be formulated in to capsules. Col. 14, lines 39-48. However, while the references teaches how to produce of secretory IgA antibodies to an antigen, it does not teach or suggest the administration of the antigen to the floor of the mouth, or specifically provide a motivation for the induction of anti-HIV IgAs.

The teachings of both Gorse and Beckenkamp have been described above. As indicated above, Gorse provides a suggestion and motivation for those in the art to induce the production of oral secretory IgA against HIV. Further, Beckenkamp indicates that such a response could be induced by administering the antigen to the floor of the mouth. Thus, these three references cumulatively render the presently claimed invention obvious.

Conclusion

19. No claims are allowed.

20. The following prior art reference is made of record and is considered pertinent to applicant's disclosure. However, while relevant it is also not used as a basis for rejection for the stated reasons.

> Bukawa et al., Nat Med, 1(7): 681-85 (1995). This reference teaches the oral administration of an HIV antigen to induce the induction of secretory IgA. However, while the reference teaches that the vaccine is administered orally, the administration is by oral intubation, and appears to induce IgA production in mucosal membranes other than the buccal membranes. Page 682 (indicating that the authors identified fecal IgA, indicating that the antibodies were likely to be from rectal mucosa).

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner

JAMES HOUSEL 11/3/03
SUPERVISORY PATENT EXAMINER
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